REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

I. CLAIM STATUS AND AMENDMENTS

Claims 1, 5-17 and 19-35 were pending in this application when last examined.

Claims 14-16, 19, 21-25 and 31-34 were withdrawn as non-elected subject matter.

Claims 1, 5-13, 17, 20, 26-30 and 35 were examined on the merits and stand rejected.

Claims 1, 5-16 and 19-35 have been cancelled without prejudice or disclaimer thereto. Applicants reserve the right to file a continuation or divisional application on any cancelled subject matter.

Claims 17 has been amended to restrict the "α-blockers" to prazosin and tamulosin as supported by Experimental Example 4 on pages 122-125 and the chemical formula for KMD-3213 as supported at page 92 of the disclosure. Support can also be found at page 90, line 23 to page 91, line 3, page 97, lines 25-30 and page 101, lines 15-20.

Therefore, no new matter has been added by this amendment.

Claim 17 is pending upon entry of this amendment.

On page 2 of the Office Action, it was indicated that the previous rejections under 112, first paragraph and 103 are maintained. However, it appears that the obviousness rejection of claims 26-30 under 35 U.S.C. § 103(a) over Goto in the Office Action of July 12, 2005 has been withdrawn, because the rejection was not made in the most recent Action.

II. OBVIOUSNESS REJECTION

In item 1 on pages 2-4 of the Office Action, claims 1, 5-13, 20, 26-30 and 35 were rejected under 35 U.S.C. § 103(a) as obvious over Goto (US 5,528,800) in view of Tobin et al. (Eur. J. Pharm., Vol. 281, pp. 1-8 (1995)) and Lai et al. (Life Science, Vol. 62, No. 13, pp. 1179-1186 (1998)).

The present amendment has cancelled the rejected claims, thereby obviating the rejection.

III. ENABLEMENT REJECTION

In item 2 on page 5 of the Office Action, claim 17 was rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification lacks enablement for a pharmaceutical composition for improving excretory potency of the urinary bladder comprising a combination of any α-blockers and any non-carbamate amine compounds having acetylcholinesterase-inhibiting action ("AchE").

The rejection is premised on the position that without guidance on what proportion of each agent to combine, mixing an α-blocker with an AchE inhibitor could be dangerous due to a potentially fatal decrease in blood pressure. It was asserted that safety and efficacy are critical factors that contribute to the unpredictability of the pharmaceutical art. The Office also argued that there is a lack of guidance in the specification for selecting a specific α-blocker in combination with the claimed compound, which can be safely used.

This rejection is respectfully traversed as applied to amended claim 17.

The test of enablement is whether one reasonably skilled in the art can make or use the invention based on the disclosure in the specification coupled with the knowledge in the art without undue experimentation. See M.P.E.P. § 2164.01.

Claim 17 has been amended to limit the α-blockers to prazosin, tamsulosin and KMD-3213. Support for the use of these specific α-blockers can be found in the specification at page

90, line 23 to page 91, line 3, page 92, page 97, lines 25-30, page 101, lines 15-20 and Experimental Example 4 on pages 122-125. Accordingly, the claim has been amended to clearly identify the specific α-blockers to be used.

First, regarding the safety and efficacy concerns, the mechanism of dysuria caused by prostatomegaly can be classified as: (1) a mechanical urethral obstruction caused by prostatomegaly; and (2) a functional urethral obstruction caused by hypertonia of smooth muscle of prostate. Treatment with anti-androgen and a surgical treatment to shrink the prostate are effective for the former. Therapy to release the tone in prostate and smooth muscle of urethra with a blocker, such as tamsulosin, which decreases urethral resistance is effective for the latter case.

Therefore, for prostatomegaly based on functional urethral obstruction, the combined use of the specific α-blocker blockers and the compound of the present invention can be expected to provide a potent improving action of urination function by decreasing urethral resistance with the α-blocker, and increasing the contraction potency of the muscle of urinary bladder with the AchE inhibitor without fear of high pressure urination. Accordingly, such combination therapy is safe and useful for treating dysuria. In fact, a synergic effect was observed in the improving activity of urination efficiency as shown in Tables 8- 9 of Experimental Example 4 of the specification.

Also, regarding the diagnosis of mechanical urethral obstruction and functional urethral obstruction, the skilled clinician can easily diagnose such by ultrasound imaging, etc. Therefore the concomitant treatment of an α-blocker and a non-carbamate AchE inhibitor does not pose a risk.

Furthermore, not withstanding that the claimed pharmaceutical is effective and safe, it is well established that safety and efficacy should are not to be confused with the requirements of patentability. The M.P.E.P. at § 2107.03, V (pages 2100-45 to 2100-46) clearly indicates that "it is improper for Office personnel to request evidence of safety in the treatment of humans, or

regarding the degree of effectiveness." Also, the M.P.E.P. at § 2164.01(c) (pages 2100-180) clearly indicates that "[t]he applicant need not demonstrate that the invention is completely safe." Thus, it is again respectfully submitted that the Office's position regarding potential safety concerns is the improper standard to apply.

Second, with regard to dosage and administration, the content of the non-carbamate amine compound having AChE inhibitory action and the dosage as a therapeutic agent for urination difficulty in a combined application with an α-blocker are described in detail on pages 108-109 of the specification.

In summary, one of skill in the art could make and safely use the claimed pharmaceutical composition comprising a combination of a specific α-blocker and the specific AchE inhibitor of the claim without undue experimentation given the guidance in the specification and the knowledge in the art.

Therefore, the rejection of claim 17 under 35 U.S.C. § 112, first paragraph, is untenable and should be withdrawn.

CONCLUSION

In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

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